PTO/PCT Rect : 0.9 AUG 2002

PATENT #4

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Irina Caminschi, et al.

Serial No.: 10/070,982

Filed: March 8, 2002

For: DENDRITIC CELL MEMBRANE

PROTEIN FIRE

Group Art Unit: Unknown

Examiner: Unknown

Atty. Dkt. No.: FBRC:011US

EXPRESS MAIL MAILING LABEL

NUMBER EL 839265725 US

DATE OF DEPOSIT August 9, 2002

SECOND PRELIMINARY AMENDMENT

BOX PCT

Commissioner for Patents Washington, D.C. 20231

Sir:

Please amend the above-identified patent application as follows:

AMENDMENT

In the specification:

Please insert as the first paragraph of the specification the following paragraph:

This is a U.S. National Application under 35 U.S.C. § 371 of International Application No. PCT/AU00/01083 filed on September 11, 2000, which claims the benefit of priority to AU PQ 2728 filed on September 9, 1999.

In the claims:

Please amend claim 1 as follows:

10/16/2002 SAHRED1 00000006 10070982

01 FC:1615 486.00 OP

25146561.1

1

1. An isolated polypeptide comprising the amino acid sequence of SEQ ID NO:1 or a functional fragment thereof or an amino acid sequence having at least 50% identity to the amino acid sequence of SEQ ID NO:1 or a functional fragment thereof.

Please add the following new claims:

- 27. (New) The isolated polypeptide of claim 1, wherein the amino acid sequence has at least 50% identity to the amino acid sequence of SEQ ID NO: 1.
- 28. (New) The isolated polypeptide of claim 27, wherein the amino acid sequence has at least 70% identity to the amino acid sequence of SEQ ID NO: 1.
- 29. (New) The isolated polypeptide of claim 27, wherein the amino acid sequence has at least 80% identity to the amino acid sequence of SEQ ID NO: 1.
- 30. (New) The isolated polypeptide of claim 27, wherein the amino acid sequence has at least 90% identity to the amino acid sequence of SEQ ID NO: 1.
- 31. (New) An isolated polypeptide comprising the amino acid sequence of SEQ ID NO:2 or a functional fragment thereof or an amino acid sequence having at least 50% identity to the amino acid sequence of SEQ ID NO:2 or a functional fragment thereof.
- 32. (New) The isolated polypeptide of claim 31, wherein the amino acid sequence has at least 50% identity to the amino acid sequence of SEQ ID NO: 2.
- 33. (New) The isolated polypeptide of claim 32, wherein the amino acid sequence has at least 70% identity to the amino acid sequence of SEQ ID NO: 2.
- 34. (New) The isolated polypeptide of claim 32, wherein the amino acid sequence has at least 80% identity to the amino acid sequence of SEQ ID NO: 2.
- 35. (New) The isolated polypeptide of claim 32, wherein the amino acid sequence has at least 90% identity to the amino acid sequence of SEQ ID NO: 2.

- 36. (New) An isolated ligand, wherein the ligand interacts with a functional fragment of SEQ ID NO: 1 or SEQ ID NO: 2.
- 37. (New) The isolated ligand of claim 36, wherein the functional fragment has at least 50% identity to the amino acid sequence of SEQ ID NO: 1 or SEQ ID NO: 2.
- 38. (New) The isolated ligand of claim 36, wherein the functional fragment has at least 70% identity to the amino acid sequence of SEQ ID NO: 1 or SEQ ID NO: 2.
- 39. (New) The isolated ligand of claim 36, wherein the functional fragment has at least 80% identity to the amino acid sequence of SEQ ID NO: 1 or SEQ ID NO: 2.
- 40. (New) The isolated ligand of claim 36, wherein the functional fragment has at least 90% identity to the amino acid sequence of SEQ ID NO: 1 or SEQ ID NO: 2.
- 41. (New) The isolated ligand of claim 36, wherein the functional fragment has the amino acid sequence of SEQ ID NO: 1 or SEQ ID NO: 2.
- 42. (New) The isolated ligand of claim 36, wherein the ligand is an antibody.
- 43. (New) The isolated ligand of claim 42, wherein the ligand is the binding portion of the antibody.
- 44. (New) An isolated nucleic acid molecule comprising the sequence of SEQ ID NO:3, a sequence having at least 60% identity to the sequence of SEQ ID NO:3, a sequence which hybridizes to the sequence of SEQ ID NO:3 under stringent conditions, or a sequence encoding a functional analogue of a polypeptide of SEQ ID NO:1.
- 45. (New) The isolated nucleic acid molecule of claim 44, wherein the nucleic acid molecule comprises a sequence of at least 60% identity with the sequence of SEQ ID NO:3.
- 46. (New) The isolated nucleic acid molecule of claim 45, wherein the nucleic acid molecule comprises a sequence of at least 70% identity with the sequence of SEQ ID NO:3.
- 47. (New) The isolated nucleic acid molecule of claim 45, wherein the nucleic acid molecule comprises a sequence of at least 80% identity with the sequence of SEQ ID NO:3.

- 48. (New) The isolated nucleic acid molecule of claim 45, wherein the nucleic acid molecule comprises a sequence of at least 90% identity with the sequence of SEQ ID NO:3.
- 49. (New) An isolated nucleic acid molecule comprising the sequence of SEQ ID NO:4, a sequence having at least 60% identity to the sequence of SEQ ID NO:, a sequence which hybridizes to the sequence of SEQ ID NO:4 under stringent conditions, or a sequence encoding a functional analogue of a polypeptide of SEQ ID NO:2.
- 50. (New) The isolated nucleic acid molecule of claim 49, wherein the nucleic acid molecule comprises a sequence of at least 60% identity with the sequence of SEQ ID NO:4.
- 51. (New) The isolated nucleic acid molecule of claim 50, wherein the nucleic acid molecule comprises a sequence of at least 70% identity with the sequence of SEQ ID NO:4.
- 52. (New) The isolated nucleic acid molecule of claim 50, wherein the nucleic acid molecule comprises a sequence of at least 80% identity with the sequence of SEQ ID NO:4.
- 53. (New) The isolated nucleic acid molecule of claim 50, wherein the nucleic acid molecule comprises a sequence of at least 90% identity with the sequence of SEQ ID NO:4.
- 54. (New) An isolated nucleic acid molecule encoding the binding region of a ligand, wherein the ligand interacts with a functional fragment of SEQ ID NO: 1 or SEQ ID NO: 2.
- 55. (New) The isolated nucleic acid molecule of claim 54, wherein the ligand is an antibody.
- (New) A composition for use in raising or lowering an immune response in a subject comprising a ligand that interacts with a functional fragment of SEQ ID NO: 1 or SEQ ID NO: 2 and an antigen.
- 57. (New) The composition of claim 56, further comprising a carrier.
- 58. (New) The composition of claim 56, further comprising an adjuvant.
- 59. (New) The composition of claim 56, further comprising an adjuvant and a carrier.
- 60. (New) The composition of claim 56, wherein the antigen is associated with the ligand.

- 61. (New) The composition of claim 56, wherein the antigen is conjugated to the ligand.
- 62. (New) A composition for use in raising or lowering an immune response in a subject comprising a nucleic acid molecule and a carrier, wherein the nucleic acid molecule comprises a first sequence encoding a ligand that interacts with a functional fragment of SEQ ID NO: 1 or SEQ ID NO: 2 and a second sequence encoding an antigen.
- 63. (New) A method of screening a putative compound for immunological regulatory activity comprising;
 - (a) reacting the compound with a polypeptide comprising the amino acid sequence of SEQ ID NO:1 or a functional fragment thereof or an amino acid sequence having at least 50% identity to the amino acid sequence of SEQ ID NO:1 or a functional fragment thereof; and
 - (b) measuring the interaction between the compound and the polypeptide.
- 64. (New) A method of isolating an antigen presenting cell from a biological sample comprising contacting the biological sample with a ligand, wherein the ligand interacts with a functional fragment of SEQ ID NO: 1 or SEQ ID NO: 2, to form a complex between the ligand and the antigen presenting cell and isolating the complex formed between the ligand and the antigen presenting cell from the biological sample.
- 65. (New) The method of claim 64, wherein the ligand is immobilized on a solid support.
- 66. (New) A method of immunizing a subject comprising:
 - (a) isolating antigen presenting cells from a fluid sample obtained from the subject, wherein the isolation involves contacting the fluid sample with a ligand that interacts with a functional fragment of SEQ ID NO: 1 or SEQ ID NO: 2;
 - (b) exposing the cells isolated from step (a) to an antigen; and
 - (c) reintroducing the cells from step (b) into the subject.

- 67. (New) The method of claim 66, further comprising the step of growing the antigen presenting cells *in vitro* after step (a).
- 68. A method of immunizing a subject comprising:
 - (a) obtaining a fluid sample from the subject;
 - isolating precursor cells from the fluid sample by contacting the fluid sample with a ligand that interacts with a functional fragment of SEQ ID NO: 1 or SEQ ID NO:
 2;
 - (c) growing the cells isolated from step (a) *in vitro* such that they mature and differentiate to become antigen presenting cells;
 - (d) exposing the cells obtained in step (c) to an antigen; and
 - (e) reintroducing the cells from step (d) into the subject.
- 69. (New) A method of modulating an immune response in a subject comprising administering to the subject a ligand that interacts with a functional fragment of SEQ ID NO: 1 or SEQ ID NO: 2 such that the ligand binds to and inhibits the function of an antigen presenting cell.
- 70. (New) The method of claim 69, wherein the antigen presenting cell is a myeloid dendritic cell.
- 71. (New) The method of claim 69, further comprising the step of administering an antigen to the subject.
- 72. (New) The method of claim 71, wherein the antigen is administered after administration of the ligand.

REMARKS

I. State of the claims

Claims 1-26 were present in the PCT application and were filed with the application on March 8, 2002. Claims 2-26 were cancelled without prejudice or disclaimer in a First Preliminary Amendment filed concurrently with the application. Applicants expressly reserved the right to pursue claims to the subject matter of claims 2-26. Applicants add by the present amendment claims 27-72. Therefore, claims 1 and 27-72 are currently pending. No new matter is introduced by these amendments.

II. Conclusion

Examination of the amended claims is respectfully requested.

Respectfully submitted,

Thomas M. Boyce Reg. No. 43,508

Attorney for Applicants

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Date:

August 9, 2002

JC13 Rec'd PCT/PTO 0 8 MAR 2002

Express Mail	Cert. No. EL794535315US	
Date:	March 8, 2002	

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE DO/EO/US RECEIVING OFFICE

Applicants for DO/EO/US:

Irina CAMINSCHI, Stephane Alain VANDENABEELE, Mark Dexter WRIGHT, Kenneth Douglas SHORTMAN

Atty. Dkt. No.: FBRC:011/TMB

International Application No.: PCT/AU00/01083

International Filing Date: 11 September 2000

Title: DENDRITIC CELL MEMBRANE PROTEIN FIRE

PRELIMINARY AMENDMENT

BOX PCT

Assistant Commissioner for Patents Washington, D.C. 20231

Sir:

Please amend the above-identified patent application as follows:

AMENDMENT

In the claims:

Please cancel without prejudice or disclaimer claims 2-26.

REMARKS

I. State of the claims

Claims 1-26 were present in the PCT application and were filed herewith. Claims 2-26

have been cancelled without prejudice or disclaimer. Applicants expressly reserve the right to

pursue claims to the subject matter of claims 2-26.

II. Conclusion

The claims have been amended to eliminate multiple dependencies. Examination of the

amended claim is respectfully requested.

No fees are believed to be due in connection with the filing of this Preliminary Amendment;

however, should any fees under 37 C.F.R §§ 1.16 to 1.21 be deemed necessary for any reason

relating to the enclosed materials, the Commissioner is hereby authorized to deduct said fees from

Fulbright & Jaworski Deposit Account No. 50-1212/10011874/TMB.

Respectfully submitted,

Thomas M. Boyce Reg. No. 43,508

Attorney for Applicants

FULBRIGHT & JAWORSKI 600 Congress Avenue, Suite 2400 Austin, Texas 78701 (512) 536-3043

Date:

March 8, 2002

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215

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- Ser Arg Asn Ile Lys Met Leu His Ile Cys Ala Phe Gly Tyr Gly Leu 705 710 715 720
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Gln Ile Gly Pro Val Ala Gly Val Met Ala Tyr Leu Phe Thr Ile Ile 820 825 830

Asn Ser Leu Gln Gly Ala Phe Ile Phe Leu Ile His Cys Leu Leu Asn 835 840 845

Gly Gln Val Arg Glu Glu Tyr Lys Arg Trp Ile Thr Gly Lys Thr Lys 850 855 860

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Thr Asp Thr Thr Asp Ser Tyr Tyr Cys Thr Cys Lys Arg Gly Phe Leu 50 55 60

Ser Ser Asn Gly Gln Thr Asn Phe Gln Gly Pro Gly Val Glu Cys Gln
65 70 75 80

Asp Val Asn Glu Cys Leu Gln Ser Asp Ser Pro Cys Gly Pro Asn Ser 85 90 95

Val Cys Thr Asn Ile Leu Gly Arg Ala Lys Cys Ser Cys Leu Arg Gly
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Phe Ser Ser Ser Thr Gly Lys Asp Trp Ile Leu Gly Ser Leu Asp Asn

Phe Leu Cys Ala Asp Val Asp Glu Cys Leu Thr Ile Gly Ile Cys Pro 130 135 140

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Gln Pro Gly Phe Val Leu Asn Gly Ser Ile Cys Glu Asp Glu Asp Glu

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Leu	Gly	Ser 195	Tyr	Tyr	Cys	Thr	Cys 200	Asn	Ser	Gly	Leu	Glu 205	Ser	Ser	Gly
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Glu 225	Cys	Ser	Arg	Asn	Ser 230	Thr	Leu	Cys	Gly	Pro 235	Thr	Phe	Ile	Cys	Ile 240
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Leu	ı Val	. Let 435	ı Glu	ı Glr	n Ala	Thr	Th:) Phe	e Glu	ı Lev	Sei 445	: Lys	: Glu	ı Glı
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Ile Lys Met Leu His Leu Cys Ala Phe Gly Tyr Gly Leu Pro Val Leu 755 760 765

Val Val Ile Ile Ser Ala Ser Val Gln Pro Arg Gly Tyr Gly Met His
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Asn Arg Cys Trp Leu Asn Thr Glu Thr Gly Phe Ile Trp Ser Phe Leu 785 790 795 800

Gly Pro Val Cys Met Ile Ile Thr Ile Asn Ser Val Leu Leu Ala Trp 805 810 815

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Ser Lys Leu Lys Asp Thr Arg Leu Leu Thr Phe Lys Ala Ile Ala Gln 835 840 845

Ile Phe Ile Leu Gly Cys Ser Trp Val Leu Gly Ile Phe Gln Ile Gly 850 855 860

Pro Leu Ala Ser Ile Met Ala Tyr Leu Phe Thr Ile Ile Asn Ser Leu 865 870 875 880

Gln Gly Ala Phe Ile Phe Leu Ile His Cys Leu Leu Asn Arg Gln Val 885 890 895

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Asn Ser Ser Cys Val Asn Ala Thr Ala Cys Arg Cys Asn Pro Gly Phe 35 40 45

Ser Ser Phe Ser Glu Ile Ile Thr Thr Pro Thr Glu Thr Cys Asp Asp 50 55 60

Ile Asn Glu Cys Ala Thr Pro Ser Lys Val Ser Cys Gly Lys Phe Ser Asp Cys Trp Asn Thr Glu Gly Ser Tyr Asp Cys Val Cys Ser Pro Gly Tyr Glu Pro Val Ser Gly Ala Lys Thr Phe Lys Asn Glu Ser Glu Asn Thr Cys Gln Asp Glu Cys Ser Ser Gly Gln His Gln Cys Asp Ser Ser Thr Val Cys Phe Asn Thr Val Gly Ser Tyr Ser Cys Arg Cys Arg Pro Gly Trp Lys Pro Arg His Gly Ile Pro Asn Asn Gln Lys Asp Thr Val Cys Glu Asp Met Thr Phe Ser Thr Trp Thr Pro Pro Pro Gly Val His 170 Ser Gln Thr Leu Ser Arg Phe Phe Asp Lys Val Gln Asp Leu Gly Arg 185 Asp Ser Lys Thr Ser Ser Ala Glu Val Thr Ile Gln Asn Val Ile Lys 200 Leu Val Asp Glu Leu Met Glu Ala Pro Gly Asp Val Glu Ala Leu Ala 215 Pro Pro Val Arg His Leu Ile Ala Thr Gln Leu Leu Ser Asn Leu Glu 230 235 Asp Ile Met Arg Ile Leu Ala Lys Ser Leu Pro Lys Gly Pro Phe Thr 245 Tyr Ile Ser Pro Ser Asn Thr Glu Leu Thr Leu Met Ile Gln Glu Arg 265 Gly Asp Lys Asn Val Thr Met Gly Gln Ser Ser Ala Arg Met Lys Leu 280 Asn Trp Ala Val Ala Ala Gly Ala Glu Asp Pro Gly Pro Ala Val Ala 295 Gly Ile Leu Ser Ile Gln Asn Met Thr Thr Leu Leu Ala Asn Ala Ser 305 Leu Asn Leu His Ser Lys Lys Gln Ala Glu Leu Glu Glu Ile Tyr Glu 330 Ser Ser Ile Arg Gly Val Gln Leu Arg Arg Leu Ser Ala Val Asn Ser

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Ile Ile Leu Ile Asn Leu Val Phe Tyr Phe Leu Ile Ile Trp Ile Leu
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Val Arg Leu Ile Val Ala Tyr Leu Phe Thr Ile Ile Asn Val Leu Gln
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Gly Val Leu Ile Phe Met Val His Cys Leu Leu Asn Arg Gln Val Arg 580 585 590

Met Glu Tyr Lys Lys Trp Phe His Arg Leu Arg Lys Glu Val Glu Ser 595 600 605

Glu Ser Thr Glu Val Ser His Ser Thr Thr His Thr Lys Met Gly Leu 610 615 620

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Ser Asp Ser Ile Leu Pro Ser Thr Glu Val Ala Gly Val Tyr Leu Ser 645 650 655

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Leu Ala Cys Phe Thr Trp Met Leu Leu Glu Gly Leu His Leu Phe Leu 385 390 395 400

Thr Val Arg Asn Leu Lys Val Ala Asn Tyr Thr Ser Thr Gly Arg Phe 405 410 415

Lys Lys Arg Phe Met Tyr Pro Val Gly Tyr Gly Ile Pro Ala Val Ile 420 425 430

Ile Ala Val Ser Ala Ile Val Gly Pro Gln Asn Tyr Gly Thr Phe Thr 435 440 445

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Phe Ile Leu Gly Cys Ser Trp Gly Leu Gly Phe Phe Met Val Glu Glu 515 520 525

Val Gly Lys Thr Ile Gly Ser Ile Ile Ala Tyr Ser Phe Thr Ile Ile 530 535 540

Asn Thr Leu Gln Gly Val Leu Leu Phe Val Val His Cys Leu Leu Asn 545 550 555 560

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Gly Val Glu Thr Glu Ser Thr Glu Met Ser Arg Ser Thr Thr Gln Thr 580 585 590

Lys Thr Glu Glu Val Gly Lys Ser Ser Glu Ile Phe His Lys Gly Gly 595 600 605

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Cys Lys Asn Leu Ser Gly Arg Tyr Lys Cys Ser Cys Leu Asp Gly Phe 105

Ser Ser Pro Thr Gly Asn Asp Trp Val Pro Gly Lys Pro Gly Asn Phe 120

Ser Cys Thr Asp Ile Asn Glu Cys Leu Thr Ser Arg Val Cys Pro Glu 135

His Ser Asp Cys Val Asn Ser Met Gly Ser Tyr Ser Cys Ser Cys Gln 150

Val Gly Phe Ile Ser Arg Asn Ser Thr Cys Glu Asp Val Asn Glu Cys 170

Ala Asp Pro Arg Ala Cys Pro Glu His Ala Thr Cys Asn Asn Thr Val

Gly Asn Tyr Ser Cys Phe Cys Asn Pro Gly Phe Glu Ser Ser Gly 200

His Leu Ser Cys Gln Gly Leu Lys Ala Ser Cys Glu Asp Ile Asp Glu

Cys Thr Glu Met Cys Pro Ile Asn Ser Thr Cys Thr Asn Thr Pro Gly 235

Ser Tyr Phe Cys Thr Cys His Pro Gly Phe Ala Pro Ser Ser Gly Gln 250

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Arg Gln Asp Pro Ser Thr Cys Gly Pro Asn Ser Ile Cys Thr Asn Ala

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250

245

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Asn Gly Gln Leu Asn Phe Lys Asp Leu Glu Val Thr Cys Glu Asp Ile 305 310 315 320

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Cys Thr Leu Val Asn Ala Thr Phe Thr Ile Leu Asp Asn Thr Cys Glu 405 410 415

Asn Lys Ser Ala Pro Val Ser Leu Gln Ser Ala Ala Thr Ser Val Ser 420 425 430

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Gly Cys Phe Ile Ile Lys Glu Ser Val Ser Thr Gly Ala Pro Gly Val 515 520 525

Ala Phe Val Ser Phe Ala His Met Glu Ser Val Leu Asn Glu Arg Phe 530 535 540

Phe Glu Asp Gly Gln Ser Phe Arg Lys Leu Arg Met Asn Ser Arg Val 545 550 555

- Val Gly Gly Thr Val Thr Gly Glu Lys Lys Glu Asp Phe Ser Lys Pro 565 570 575
- Ile Ile Tyr Thr Leu Gln His Ile Gln Pro Lys Gln Lys Ser Glu Arg 580 585 590
- Pro Ile Cys Val Ser Trp Asn Thr Asp Val Glu Asp Gly Arg Trp Thr 595 600 605
- Pro Ser Gly Cys Glu Ile Val Glu Ala Ser Glu Thr His Thr Val Cys 610 615 620
- Ser Cys Asn Arg Met Ala Asn Leu Ala Ile Ile Met Ala Ser Gly Glu 625 630 635
- Leu Thr Met Glu Phe Ser Leu Tyr Ile Ile Ser His Val Gly Thr Val
- Ile Ser Leu Val Cys Leu Ala Leu Ala Ile Ala Thr Phe Leu Leu Cys
 660 665 670
- Arg Ala Val Gln Asn His Asn Thr Tyr Met His Leu His Leu Cys Val 675 680 685
- Cys Leu Phe Leu Ala Lys Ile Leu Phe Leu Thr Gly Ile Asp Lys Thr 690 695 700
- Asp Asn Gln Thr Ala Cys Ala Ile Ile Ala Gly Phe Leu His Tyr Leu 705 710 715 720
- Phe Leu Ala Cys Phe Phe Trp Met Leu Val Glu Ala Val Met Leu Phe 725 730 735
- Leu Met Val Arg Asn Leu Lys Val Val Asn Tyr Phe Ser Ser Arg Asn 740 745 750
- Ile Lys Met Leu His Leu Cys Ala Phe Gly Tyr Gly Leu Pro Val Leu 755 760 765
- Val Val Ile Ile Ser Ala Ser Val Gln Pro Arg Gly Tyr Gly Met His 770 775 780
- Asn Arg Cys Trp Leu Asn Thr Glu Thr Gly Phe Ile Trp Ser Phe Leu 785 790 795 800
- Gly Pro Val Cys Met Ile Ile Thr Ile Asn Ser Val Leu Leu Ala Trp 805 810 815
- Thr Leu Trp Val Leu Arg Gln Lys Leu Cys Ser Val Ser Ser Glu Val 820 825 830
- Ser Lys Leu Lys Asp Thr Arg Leu Leu Thr Phe Lys Ala Ile Ala Gln 835 840 845
- Ile Phe Ile Leu Gly Cys Ser Trp Val Leu Gly Ile Phe Gln Ile Gly 850 855 860

Pro Leu Ala Ser Ile Met Ala Tyr Leu Phe Thr Ile Ile Asn Ser Leu 865 870 875 880

Gln Gly Ala Phe Ile Phe Leu Ile His Cys Leu Leu Asn Arg Gln Val 885 890 895

Arg Asp Glu Tyr Lys Lys Leu Leu Thr Arg Lys Thr Asp Leu Ser Ser 900 905 910

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Ser Ser Phe Ser Glu Ile Ile Thr Thr Pro Thr Glu Thr Cys Asp Asp 50 55 60

Ile Asn Glu Cys Ala Thr Pro Ser Lys Val Ser Cys Gly Lys Phe Ser 65 70 75 80

Asp Cys Trp Asn Thr Glu Gly Ser Tyr Asp Cys Val Cys Ser Pro Gly
85 90 95

Tyr Glu Pro Val Ser Gly Ala Lys Thr Phe Lys Asn Glu Ser Glu Asn 100 105 110

Thr Cys Gln Asp Glu Cys Ser Ser Gly Gln His Gln Cys Asp Ser Ser 115 120 125

Thr Val Cys Phe Asn Thr Val Gly Ser Tyr Ser Cys Arg Cys Arg Pro 130 135 140

Gly Trp Lys Pro Arg His Gly Ile Pro Asn Asn Gln Lys Asp Thr Val 145 150 155 160

Cys Glu Asp Met Thr Phe Ser Thr Trp Thr Pro Pro Pro Gly Val His
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Ser Gln Thr Leu Ser Arg Phe Phe Asp Lys Val Gln Asp Leu Gly Arg 180 185 190

- Asp Ser Lys Thr Ser Ser Ala Glu Val Thr Ile Gln Asn Val Ile Lys 195 200 205
- Leu Val Asp Glu Leu Met Glu Ala Pro Gly Asp Val Glu Ala Leu Ala 210 215 220
- Pro Pro Val Arg His Leu Ile Ala Thr Gln Leu Leu Ser Asn Leu Glu 225 230 235 240
- Asp Ile Met Arg Ile Leu Ala Lys Ser Leu Pro Lys Gly Pro Phe Thr 245 250 255
- Tyr Ile Ser Pro Ser Asn Thr Glu Leu Thr Leu Met Ile Gln Glu Arg 260 265 270
- Gly Asp Lys Asn Val Thr Met Gly Gln Ser Ser Ala Arg Met Lys Leu 275 280 285
- Asn Trp Ala Val Ala Ala Gly Ala Glu Asp Pro Gly Pro Ala Val Ala 290 295 300
- Gly Ile Leu Ser Ile Gln Asn Met Thr Thr Leu Leu Ala Asn Ala Ser 305 310 315
- Leu Asn Leu His Ser Lys Lys Gln Ala Glu Leu Glu Glu Ile Tyr Glu 325 330 335
- Ser Ser Ile Arg Gly Val Gln Leu Arg Arg Leu Ser Ala Val Asn Ser 340 345 350
- Ile Phe Leu Ser His Asn Asn Thr Lys Glu Leu Asn Ser Pro Ile Leu 355 360 365
- Phe Ala Phe Ser His Leu Glu Ser Ser Asp Gly Glu Ala Gly Arg Asp 370 375 380
- Pro Pro Ala Lys Asp Val Met Pro Gly Pro Arg Gln Glu Leu Leu Cys 385 390 395
- Ala Phe Trp Lys Ser Asp Ser Asp Arg Gly Gly His Trp Ala Thr Glu 405 410 415
- Val Cys Gln Val Leu Gly Ser Lys Asn Gly Ser Thr Thr Cys Gln Cys 420 425 430
- Ser His Leu Ser Ser Phe Thr Ile Leu Met Ala His Tyr Asp Val Glu 435 440 445
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- Phe Cys Leu Leu Cys Ile Leu Thr Phe Leu Leu Val Arg Pro Ile 465 470 475 480
- Gln Gly Ser Arg Thr Thr Ile His Leu His Leu Cys Ile Cys Leu Phe 485 490 495

Val Gly Ser Thr Ile Phe Leu Ala Gly Ile Glu Asn Glu Gly Gln 500 505 510

Val Gly Leu Arg Cys Arg Leu Val Ala Gly Leu Leu His Tyr Cys Phe 515 520 525

Leu Ala Ala Phe Cys Trp Met Ser Leu Glu Gly Leu Glu Leu Tyr Phe
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Leu Val Val Arg Val Phe Gln Gly Gln Gly Leu Ser Thr Arg Trp Leu 545 550 555 560

Cys Leu Ile Gly Tyr Gly Val Pro Leu Leu Ile Val Gly Val Ser Ala
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Ala Ile Tyr Ser Lys Gly Tyr Gly Arg Pro Arg Tyr Cys Trp Leu Asp 580 585 590

Phe Glu Gln Gly Phe Leu Trp Ser Phe Leu Gly Pro Val Thr Phe Ile 595 600 605

Ile Leu Cys Asn Ala Val Ile Phe Val Thr Thr Val Trp Lys Leu Thr 610 615 620

Gln Lys Phe Ser Glu Ile Asn Pro Asp Met Lys Lys Leu Lys Lys Ala 625 630 635 640

Arg Ala Leu Thr Ile Thr Ala Ile Ala Gln Leu Phe Leu Leu Gly Cys 645 650 655

Thr Trp Val Phe Gly Leu Phe Ile Phe Asp Asp Arg Ser Leu Val Leu 660 665 670

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Leu Leu His Cys Leu Leu Asn Lys Lys Val Arg Glu Glu Tyr Arg Lys
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